REMARKS

CONTINUED EXAMINATION

Applicants thank the Examiner for entering Applicants' submission dated 02/26/2007 and for withdrawing the finality of the previous Office Action in accordance with 37 C.F.R. §1.114. Additionally, Applicants acknowledge the Examiner's withdrawal of the 35 US.C. §112, first paragraph, rejection in view of Applicants' previously filed amendment.

SUPPORT FOR AMENDMENT

Support for the amendment of claims **91**, **93**, **95**, **97**, **99**, and **101** may be found in Applicants' claims and specification as originally filed. Accordingly, no new matter has been introduced.

35 USC § 103(a)

Claims **91-92** stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Katz *et al.* (US 5,952,392) in view of Sintov *et al.* (WO 9602244 A1), and further in view of Arquette *et al.* (WO 9920224). Further, claims **93-102** stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Katz *et al.* (US 5,952,392) in view of Sintov *et al.* (WO 9602244 A1), in view of Arquette *et al.* (WO 9920224), and further in view of Katz (4,784,794) or Katz (5,070,107).

Applicants respectfully traverse these rejections. Applicants further submit that a *prima facie* case of obviousness has not been established.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art. MPEP § 2143.01. Second, there must be a reasonable

expectation of success to modify or combine the cited references to achieve the claimed invention. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See* MPEP § 2143. Additionally, the teaching or suggestion to make the claimed combination and the reasonable expectation of success cannot be based solely on Applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *See also* Memorandum of 03 May 2007 from Margaret A. Focarino to USPTO Technology Center Directors regarding Supreme Court decision on *KSR Int'l. Co., v. Teleflex, Inc.*

Following the Supreme Court's *KSR* decision, a number of precedential opinions by Board of Patent Appeals and Interferences (BPAI), as well as revised Examination Guidelines published by the United States Patent Office, have set out a slightly different legal standard for obviousness than that stated in the current version of the MPEP. With specific reference to the instant application, the proposed combination of purported prior art elements according to their established functions to produce the claimed invention may not be viewed as predictable. *See Ex parte Mary Smith*, Appeal 2007-1925, Application No. 09/391,869, decided 25 June 2007; *Examination Guidelines for Determining Obviousness Under 35 U.S.C. § 103 in View of the Supreme Court Decision in KSR International Co. v. Teleflex Inc.*

Claims 91-92

The Examiner proposes that Katz *et al.* (U.S. 5,952,392) "discloses that long chain fatty acids broadly including oleic acid (C18, one double bond, see col. 2 lines 12-15; col. 3, lines 5-8, col. 4, lines 26-28; col. 6, lines 28-35) or monounsaturated long chain alcohols broadly (e.g., C18-C28, or octadecenol, docosenol, brassidyl alcohol) in their effective amounts with a physiologically compatible carrier (*e.g.*, cream or ointment applied to skin, or aqueous solution, *see* col. 12, Example 5; Examples 12, 14-15, col.20, lines 34-35, and col. 22, lines 39-40 and 64) are useful in a pharmaceutical composition for topical application, intramuscular and intravenous injections, and methods of treating viral infections and virus-induced and inflammatory disease of skin and membranes because these compounds have antiviral activity *See* abstract, col. 1, lines 10-15 and 20-47; col. 3, lines 18-21; col.7, lines 62-67; col. 12, EXAMPLE 5; Examples 14-15 and col. 22-23." The Examiner further proposes that "compositions therein for use in treating viral infections comprise active ingredients [*sic*] or combination of compounds as the active ingredients selected from a group consisting of saturated aliphatic alcohols, mono-unsaturated aliphatic alcohols, mono-unsaturated aliphatic

amides and aliphatic acids having a carbon chain length of 18-28 carbons, wherein the active ingredient is present in an amount of 0.1 to about 50% by weight of the final composition. *See* column 6, lines 28-36, lines 50-55. It is taught that the compositions therein are administered to the skin or a mucous membrane topically parenterally or by transmembranal penetration using a cream, lotion, gel, ointment, suspension, aerosol spray or semi-solid formulation (*e.g.*, a suppository). *See* column 7, lines 62-67; column 24, claims 7-11."

However, Katz *et al.* (U.S. 5,952,392) does **not** disclose or teach use of "a method for treating at least one of virus-induced and inflammatory diseases, said method comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms" as required by claim **91** of the present invention. Further, Katz *et al.* (U.S. 5,952,392) **does not teach or disclose use of *any* salts of fatty acids or mixed esters in a topical composition, let alone the salts of fatty acids and mixed esters of the instant invention *in combination with* monounsaturated long chain alcohols for treating virus-induced and inflammatory disease in accordance with the present invention**. In fact, the Examiner later admits as much by stating "[t]he prior art does not expressly disclose the employment of monounsaturated long chain alcohols in combination with long chain fatty acids salts, and fatty acid esters herein in a composition for treating virus-induced and inflammatory disease of skin and membranes", (emphasis in original).

Next, the Examiner proposes that "Sintov *et al.* discloses topical pharmaceutical compositions [*sic*] for the treatment of viral infections comprising salts of carboxylic acid such as alkali metal oleates. *See* abstract; page 2, bottom paragraph; page 3, lines 1-3, paragraph 5; page 7, EXAMPLE 1." However, Sintov *et al.* does not disclose "a method for treating at least one of virus-induced and inflammatory diseases, said method comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an

admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms" as required by claim **91** of the present invention. In fact, the Sintov *et al.* reference explicitly teaches away from the use of other "any other antiviral agent" in combination with carboxylic acid salt in the treatment of viral diseases. *See* page 1, last paragraph. Sintov *et al.* **does not teach or disclose use of *any* long chain monounsaturated alcohols or mixed esters in a topical composition, let alone the monounsaturated long chain alcohols and mixed esters of the instant invention *in combination with* salts of fatty acids in accordance with the present invention.** Moreover, the Examiner later admits as much in by stating "[t]he prior art does not expressly disclose the employment of monounsaturated long chain alcohols in combination with long chain fatty acids salts, and fatty acid esters herein in a composition for treating virus-induced and inflammatory disease of skin and membranes". (emphasis in original).

Further, the salts of fatty acids in Sintov *et al.* are different from the salts of fatty acids as presented in claim **91** as amended. Specifically, Sintov *et al.*, page 2 last paragraph, states "the present invention provides a topical pharmaceutical composition wherein said salt is selected from the group consisting of linoleates, elaidates, palitates, myristates, oleaates, malonates, succinates, adipates, pimelates, maleates, fumarates or azelates." None of these salts comprise "a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion." For example, linoleates are polyunsaturated, methylene interrupted salts of 18 carbon chain length fatty acids. The salts of the present invention comprise salts of long chain fatty acids with carbon chain length of 20 or greater.

Elaidates are salts of fatty acids with all trans-double bonds. The salts of long chain fatty acids of the present invention are "trans-free". *See* forthcoming 37 C.F.R. §1.132 Affidavits of Robert Kleiman and David Ashley.

Palmitates are salts of fatty acids with a carbon chain length of 16. Myristates are salts of fatty acids with a carbon chain length of 14. Oleates are salts of fatty acids with a carbon chain

length of 18. By contrast, the present invention comprises salts of long chain fatty acids with carbon chain lengths of 20 or greater, as required by claim **91**, as amended.

Further, malonates are 3-carbon di-basic acids, succinates are saturated 4-carbon di-basic acids, adipates are 6-carbon di-basic acids, and pimelates are 7-carbon di-basic acids. The salts of the present invention comprise salts of long chain fatty acids with carbon chain lengths of 20 or greater and are mono-basic in nature.

Maleates are 4-carbon di-basic acids that are mono-unsaturated, fumarates are the trans-isomer of maleates and are also 4-carbon dibasic acids that are mono-unsaturated, and azelates are saturated di-basic acids with a 9 carbon chain length. By contrast, the salts of the present invention comprise salts of long chain fatty acids that are carbon chain lengths of 20 or greater, are mono-basic in nature, and are trans-free, in accordance with claim **91** as amended.

Moreover, Sintov *et al.* actually teaches away from the salts in the present invention by stating that "[e]specially preferred for use in the present invention is a water-solubilized C_{16}-C_{18} carboxylic acid salt, such as akali oleate." The salts of the present invention comprise salts of long chain fatty acids that are carbon chain lengths of 20 or greater. It is well known that salts of long-chain fatty acids are less soluble in water as compared with shorter chain fatty acids salts, and therefore it would be unexpected that salts with chain lengths greater than 18 carbons would have similar and/or improved activity relative to the more-water-soluble materials, such as those materials suggested in Sintov *et al.* *See* forthcoming 37 C.F.R. § 1.132 Affidavits by Robert Kleiman and David Ashley.

In regard to Arquette *et al.* (WO 9920224), the Examiner proposes that Arquette *et al.* "discloses a pharmaceutical composition comprising the instant fatty alcohols at least 10% by weight (see particularly abstract and page 3 lines 15-22), and the instant fatty acid esters in their various percentages (see pages 4-8) with a physiologically compatible carrier for topical applications (see abstract and claims 1-12, especially claim 23). It is also taught that fatty acids such as oleic acid, myristic acid etc are used as emollients. *See* page 1, lines 24-29." However, Arquette *et al.* does not disclose "a method for treating at least one of virus-induced and inflammatory diseases, said method comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according

to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2 comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms" as required by claim **91** of the present invention. In fact, Arquette *et al.* **does not teach or disclose use of *any* salts of fatty acids in a topical composition, let alone the salts of fatty acids of the instant invention *in combination with* monounsaturated long chain alcohols and mixed esters in accordance with the present invention.**

The Examiner then asserts "[I]t would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the monounsaturated long chain alcohols in combination with the long chain fatty acid salt such as alkali metal oleate in a pharmaceutical composition, in methods for treating virus-induced and inflammatory disease of skin and membranes". This assertion is irrelevant and *non sequitur* in regard to the combination of monounsaturated long chain alcohols, salts of long chain fatty acids **in combination with** mixed esters in accordance with the present invention.

The Examiner further asserts: "[O]ne having ordinary skill in the art at the time the invention was made would have been motivated to employ the instant monounsaturated long chain alcohols in combination with long chain fatty acid salts such as alkali metal oleate in a pharmaceutical composition because all active composition components monounsaturated long chain alcohols, and alkali metal salt of fatty acids such as alkali metal salt of oleic acid are known to be useful to treat virus-induced and inflammatory disease of skin and membranes according to Katz *et al.* (5,952,392) and Sintov *et al.*" Again, Applicant respectfully submits that this assertion is both irrelevant and *non sequitur* in regard to the combination of monounsaturated long chain alcohols, salts of long chain fatty acids **in combination with** mixed esters in accordance with the present invention.

The Examiner's subsequent assertion is that "it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive effects would have been reasonably expected. *See In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980)." It is important to note that the proposition in *In re Kerkhoven* is that "it is prima facie obvious to combine two compositions each of which is taught by the prior art to be

useful for the same purpose, in order to form a third composition to be used for the very same purpose…[t]he idea of combining them flow logically from their having been individually taught in the prior art." MPEP §2144.06 (citing *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)). In the instant case, the individual components of monounsaturated alcohols, salts of fatty acids, and mixed esters of the present invention were **not** taught in the prior art.

None of the references cited by the Examiner teach or disclose the salts of long chain fatty acids that are carbon chain lengths of 20 or greater, are mono-basic in nature, and are trans-free, as required by claim **91** as amended. In fact, the only reference the Examiner provides for the use of salts of fatty acids in treating viral diseases expressly teaches away from the use of salts of long chain fatty acids that are carbon chain lengths of 20 or greater, and implicitly teaches away from the combination of salts of long chain fatty acids in combination with monounsaturated alcohols and mixed esters in accordance with the present invention.

Therefore, the proposition in *In re Kerkhoven,* in conjunction with the references provided by the Examiner, may not properly be applied against claim **91** as amended.

Next, the Examiner asserts that "it would have been obvious to a person of ordinary skill in the art at the time of the invention to add instantly claimed fatty acid esters to the composition comprising monounsaturated long chain alcohols, and alkali metal salt of oleic acid because Arquette *et al.* teaches that the instantly claimed fatty acid esters are known to be used as emollients in pharmaceutical compositions". This assertion is *non sequitur* in view of claim **91** as amended, as alkali metal salts of oleic acid are not within the scope of the salts of fatty acids of the present invention; and moreover, the combination of salts with monounsaturated alcohols and mixed fatty acid esters is not taught in the references provided by the Examiner, nor does the Examiner provide reference to general knowledge of the skilled artisan. Further, the combination of the present invention for the purpose of treatment of viral and inflammatory diseases is also not taught or suggested in the references provided by the Examiner, or in the general knowledge of the skilled artisan.

The Examiner goes on to assert that "one of ordinary skill in the art at the time of the invention would have been motivated to add the instantly claimed fatty acid esters taught by Arquette *et al.* to the composition comprising monounsaturated long chain alcohols, and salt of oleic acid with reasonable expectation of obtaining a pharmaceutical composition for treating virus-

induced and inflammatory disease of skin and membranes since salts of long chain fatty acids broadly or monounsaturated long chain alcohols broadly in their effective amounts are known to be useful in pharmaceutical compositions [...] because these compounds have antiviral activity based on Katz *et al.*, and Sintov *et al.*"

As discussed above, Sintov *et al.* does not teach or suggest the salts of fatty acids in claim **91** as amended. Rather, Sintov *et al.* teaches away from the present invention by suggesting that salts of fatty acids with chain lengths of 18 or fewer carbons are preferred. Moreover, neither Sintov *et al.* or any of the other references cited by the Examiner teach the combination of the present invention for use as an effective antiviral treatment.

Therefore, the Examiner's next proposition is flawed. Specifically, the Examiner asserts that "[t]herefore one of ordinary skill in the art would have reasonably expected that combining the instant fatty acid esters taught by Arquette *et al.* with the monounsaturated fatty alcohols, and the salts of oleic acid in a pharmaceutical composition would improve the therapeutic effect for treating virus-induced and inflammatory disease of skin and membranes because 1) fatty acid esters are known to be used as an emollient [*sic*] in pharmaceutical composition comprising monounsaturated long chain alcohols, and 2) further according to Arquette emollients have beneficial effects such as softening, smoothening skin, reduce skin roughness, cracking and irritation of skin. Thus, one of ordinary skill in the art would have reasonably expected that the combination of the instant fatty acid esters taught by Arquette *et al.* with the instant fatty alcohols, and the salts of oleic acid, *i.e.*, instant salts of fatty acids in a pharmaceutical composition would have at least additive therapeutic effects, and also provide additional benefits such as softening, smoothening of skin."

The combination of fatty acid esters of Arquette *et al.*, fatty alcohols and salts of oleic acid to provide therapeutic effects does not teach or suggest the present invention. Specifically, "a method for treating at least one of virus-induced and inflammatory diseases, said method comprising the step of providing a topical composition consisting essentially of: at least one of octadecenol, eicosenol, docosenol, tetracosenol and hexacosenol in a concentration of from 0.1 to 25 percent by weight of an admixed physiologically active carrier; at least one salt of a jojoba-derived trans-free fatty acid according to the formula R^1-COO^-M^+, wherein: R^1 comprises $CH_3(CH_2)_7CH{=}CHCH_2(CH_2)_x$; x is at least one of 8, 10, and 12; and M^+ is a monovalent alkali metal ion; and at least one mixed ester according to the formula R^2-COO-R^3, wherein: R^2

comprises $CH_3(CH_2)_7CH=CHCH_2(CH_2)_y$; y is at least one of 6, 8, 10 and 12; and R^3 is at least one of an alkyl group and an aliphatic group comprising between 1 to 12 carbon atoms", as required by claim **91** as amended. Moreover, the suggested combination that the Examiner puts forth does not appreciate the surprising, synergistic effects of the combination of the present invention. *See* forthcoming 37 C.F.R. § 1.132 Affidavits of Robert Kleiman and David Ashley (discussing the 100-fold increase in antiviral activity of the present invention as compared to the antiviral activity of the alcohol alone).

As in the instant case, where the Examiner does not provide any teaching or reference for the claimed combination, nor an explanation as to how the unexpected, synergistic results of the claimed combination could be predictable, an obviousness rejection cannot be proper. Therefore, Applicants respectfully request that the rejections of claims **91-92** as amended under §103 be withdrawn.

Claims 93-102

*Applicants hereby incorporate and reiterate all arguments/remarks made under the previous section relating to the rejection of claims **91-92** under §103 in this section.*

The Examiner asserts the following:

"Katz *et al.* (5,952,392) does not explicitly teach the effective amount of the monounsaturated alcohol as from about 0.1 mg to about 2gm per 50 kg of body weight.

Katz *et al.* (4,874,794) discloses that the effective amounts of long chain fatty alcohols broadly (*e.g.*, C20-C26) with a physiologically compatible carrier in a pharmaceutical composition for topical application for methods of treating viral infections and skin inflammations are 0.1 to 25 percent by weight. See abstract, col.3, lines 63-8, claims 1-2.

Katz *et al.* (5,070,107) discloses that the effective amounts of long chain fatty alcohols broadly (*e.g.*, C27-C32) with a physiologically compatible carrier in a pharmaceutical composition for topical application and intramuscular intravenous injections for methods of treating viral infections and skin inflammations are 0.1 mg to 2 g/per 50kg of body weight. See abstract, co.3 lines 63-68, claims 1-2.

One of ordinary skill in the art would have been motivated to optimize the effective amounts of instantly claimed long chain monounsaturated alcohols in the composition because Katz *et al.* '794, and '107 teaches effective amounts of structurally similar long chain fatty alcohols active agents for treating viral infections and skin inflammations as 0.1 mg to 2 g/per 50 kg of body weight. Further, it has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients in a composition in order to achieve a beneficial effect. *See In re Boesch,* 205 USPQ 215 (CCPA 1980)."

Applicants respectfully submit that optimizing the teachings of Katz *et al.* ('392, '794, '107) references would not result in the combination of the present invention. As discussed at length above, the combination of the present invention could not have been deduced from the prior art, nor was the nature of the synergistic effect of the combination of the present invention known or appreciated in the prior art. *See* forthcoming 37 C.F.R. § 1.132 Affidavits of Robert Kleiman and David Ashley. Specifically, data presented in the 1.132 affidavits show an at least 100-fold increase in antiviral effectiveness against the HSV-1 strain (6343). *Even if* the components of the combination of the present invention were taught separately, the resulting combination could not have been characterized as merely an optimization of parameters to obtain a "beneficial effect" in accordance with *In re Boesch.*

Thus, the Examiner's proposition that an optimization of parameters of compositions taught in the prior art could account for the 100-fold increase in antiviral activity seen as a result of the combination of the present invention fails on two counts: 1) prior art does not teach the composition of the present invention (*see discussion above*) and 2) the resulting effect of the combination of the present invention is more than beneficial, rather it is more aptly characterized as synergistic and surprising. *See* forthcoming 37 C.F.R. § 1.132 Affidavits of Robert Kleiman and David Ashley.

As in the instant case, where the Examiner does not provide any teaching or reference for the claimed combination, nor an explanation as to how the unexpected, synergistic results of the claimed combination could be predictable, an obviousness rejection cannot be proper applied. Therefore, Applicants respectfully request that the rejections of claims **93-102** as amended under §103 be withdrawn.

CONCLUSION

The remaining cited references (if any) have been reviewed and are not believed to affect the patentability of the claims as amended. Claims **91** - **102** are pending in the application. Consideration and allowance of all pending claims **91** - **102** is earnestly requested.

No amendment made herein was related to the statutory requirements of patentability unless expressly stated; rather any amendment not so identified may be considered as directed *inter alia* to clarification of the structure and/or function of the invention and Applicants' best mode for practicing the same. Additionally, no amendment made herein was presented for the purpose of narrowing the scope of any claim, unless Applicants have argued that such amendment was made to distinguish over a particular reference or combination of references. Furthermore, no election to pursue a particular line of argument was made herein at the expense of precluding or otherwise impeding Applicants from raising alternative lines of argument later during prosecution. Applicants' failure to affirmatively assert specific arguments is not intended to be construed as an admission to any particular point raised by the Examiner.

Should the Examiner have any questions regarding this Response and Amendment, or feel that a telephone call to the undersigned would be helpful to advance prosecution of this matter, the Examiner is invited to call the undersigned at the number given below.

Respectfully submitted,
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